SPECTRAL ENTROPY SIGNATURE OF SPEECH PERTURBATION IN ADULT ACQUIRED GROWTH HORMONE DEFICIENCY

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Abstract: Approximate entropy (ApEn) adapted to quantify the pattern complexity across the electroglottogram (EGG) spectral domain characterizes normal male vowel phonation in two groups, a majority group (G1) with high ApEn and a minority group (G2) with low ApEn. Using the ApEn measure of normality a sample of post-treatment male oncology patients with adult onset growth hormone deficiency (GHD) shows distinctive spectral entropy signatures. These are consistent with either disrupted larynx development in relative youth, with high normal-group G1 complexity and elevated pitch, or loss of conscious control in middle age, with low normal group G2 or worse complexity. This is at least initial evidence that speech perturbation may be of value in detecting the adult GHD in oncology.

Keywords : Speech, Complexity, Endocrine, Disruption, Oncology

I. INTRODUCTION

It is well known that severe growth hormone deficiency (GHD) has a substantial impact on the growth of children and is subsequently reflected in a pronounced deficit of skeletal mass in adult life. It is perhaps less well known that GHD, acquired as an adult, strongly affects body composition as well as the continued health of the skeleton, cardiovascular risk and quality of life. In the context of quality of life in adult acquired GHD there is anecdotal evidence that subtle speech perturbation becomes noticeable but the quality of the perturbation depends on the timing of the onset of GHD. Thus we have conducted objective speech studies in four adult male oncology patients who acquired GHD in adult life. The group was measured against normal voicing adult male and female cohorts using a single-parameter measure of normality, which has recently been developed [1]. It was felt that such a study would provide useful information regarding the impact of GHD status on the development of the larynx and maintenance of speech pattern. In particular it is hoped that this will be the first stage in identifying the speech-perturbation signature of GHD.

By concentrating on vocal fold functionality a single parameter measure of normality has been developed by scientists at North Western Medical Physics in Manchester. It has been used to identify very tight bounds for ‘normal’ vowel production, or phonation, in both the healthy male and female populations. It is uniquely based on the quantification of the complexity of the entire spectral pattern from trans-larynx impedance measurements acquired during vowel phonation. The spectral pattern complexity for larynx cancer patients has been shown to be quite different and to change with the time elapsed following treatment [1]. Therefore, it is likely that complexity also has the potential to characterise subtle deviations from normal phonation resulting from GHD at different times of onset in adult life.

II. THEORY

The anterior pituitary hormone somatotrophin, commonly referred to as growth hormone, is involved in the stimulation of protein synthesis, amino-acid transport, fat and calcium uptake. Consequently, GHD in adults, regardless of gender, can result in decreased muscle mass, increased body fat and reduced bone density. In males the hormone testosterone is central to development of the adult male characteristics of musculature, bone mass, fat distribution, hair patterns, laryngeal enlargement, and vocal chord thickening. Once again pituitary disruption affects testosterone secretion. Consequently male oncology patients with GHD can be prescribed endocrine replacement therapies that include testosterone and the endocrine stimulant thyroxine.

The mass and composition of the folds, the integrity and mobility of the epithelium etc. are all reflected in the intricate pattern of fold vibration. Hence, it is possible that the vibration of the vocal folds is sensitive to minute
physiological changes [2] of the kind that might be expected in the development of GHD. Fold vibration can be measured indirectly and non-invasively by exploiting trans-larynx electrical impedance variations [3]. A time series of impedance measurements is termed the electro-glottogram or EGG. A carefully gathered EGG is free from the complex resonant effects of the vocal tract, which can be variably configured by an individual. The relatively simple EGG time series is ideal for power spectral density (PSD) analysis, which is the natural choice for investigating vibration phenomena [4,5] including the EGG [6]. However, the usefulness of conventional PSD analysis is limited by the difficulty of interpreting the spectrum taken as a whole, especially where any perturbations are subtle.

In order to quantify subtle changes to fold functionality a measure of continuous spectral pattern complexity is required, which takes into account the entire spectral domain, rather than the selective analysis of a few discrete spectral peaks that are assumed to be of paramount importance. To progress towards characterization of spectral pattern, pre-normalisation can ameliorate the effects of pitch, f_o, variation that would otherwise obscure any underlying spectral pattern in vowel phonation. Tracking f_o and expressing spectral components relative to f_o, combined with the normalisation of all component spectral powers, relative to the power of f_o, ensures that multiple spectral estimates can be averaged to reinforce common patterns. The authors term this ‘Fundamental Harmonic Normalisation’ [6]. For FHN-normalised spectra the influence of f_o power is not lost, instead it is directly reflected across the scaled pattern of the normalised spectrum itself.

‘Approximate entropy’ is a measure of time series complexity that has been used in ECG studies of anaesthetised patients [7]. The measure is sensitive to noise in the time domain. However, in the spectral domain noise is relatively slowly varying, potentially flat, and does not directly distract from the complexity analysis of features of real interest. For this reason the authors have extended complexity analysis into the EGG, FHN-spectral domain for GHD patients. Since it is normalized, the pattern complexity of the FHN spectrum is concentrated from the first maximum of the harmonic peaks onwards. Therefore, for this study the FHN spectrum was truncated and the 7 harmonics following the first FHN spectral minimum selected for analysis. After taking the logarithm of the spectrum the standard deviation, σ, of the resultant spectral series is computed for use in approximate entropy calculations.

This study uses a specific formulation of approximate entropy ApEn described by Pincus [8]. Given N data points \{u(i)\}=u(1),u(2),...,u(N) and commencing with the i\textsuperscript{th} point, vector sequences x(1) to x(N-m+1) are formed consisting of m consecutive u x(i)=\{u(i),...,u(i+m-1)\}. Then the vector sequence, x(1),x(2),...,x(N-m+1) is used to construct C\textsuperscript{m,i}(r) values for each i ≤ (N-m+1) where;

\[
C\textsuperscript{m,i}(r) = \text{number of } j \leq (N-m+1)
\]

such that \(d[x(i),x(j)]/(N-m+1) \leq r\) (1)

Where \(d[x(i),x(j)]\) in (1) is the distance between vectors, defined as the maximum difference in their scalar components. The \(C\textsuperscript{m,i}(r)\) values measure, within a tolerance r, the regularity or frequency of sequences occurring in the data set \{u(i)\}, which are similar to the given sequence, x(i) of length m. The Pincus approximate entropy statistic is then defined by;

\[
\sigma_p En = -(N-m)^{-1}\sum_{i=1}^{N-m}\ln \frac{C\textsuperscript{m,i+1}(r)}{C\textsuperscript{m,i}(r)}
\] (2)

Equation (2) is interpreted heuristically as a measure of the average logarithmic likelihood, over all sequences x(1) to x(N-m+1), that any sequence in the data series \{u(i)\}, which is within a tolerance r of the given sequence x(i) of length m, remains within the same tolerance when the length of both sequences is increased by one data point. Tolerance r is proportional to the measured series standard deviation σ, i.e. r=κσ, where k is a constant. It is necessary to empirically determine k so that the widest range of complexity values is achieved.

III. METHODOLOGY

4 adult males (age range 23-47) who had acquired their GH deficiency in adult life, either as a consequence of tumour mass effect or radiation induced damage, were studied using a Laryngograph. Details are shown in Table-1. All had adult onset GHD for at least 2 years prior to the study and were assessed several years after diagnosis of the tumour mass or treatment. 89 healthy male volunteers were recruited to provide a ‘normal’ reference Laryngographic standard. Four volunteers were excluded because of errors during capture. For pathological and normal volunteers cases Laryngograph throat sensors were used to measure trans-larynx EGG signals for the sustained vowel /i/. Sampling was at 20 kHz for up to 4 seconds. The resultant 4 pathological and 85 normal binary LX data-files were transmitted by FTP.
to a COMPAQ Unix Alpha-server-2000 dual 4/275 processor system for storage. Visualisation, spectral and complexity analysis were then performed off-line on an AMD-Athlon, 1GHz processor, NT-PC equipped with 1Gbyte memory. All software utilities were written in Research Systems International IDL 5.5.

For sustained EGG signals multiple power spectral estimates were generated for individuals by segmenting the EGG data-stream into short frames of 1000 sample points. For each frame \( f_0 \) was determined using the autocovariance function before power spectral density (PSD) computation by variance reduction and Fourier transformation. The frame PSD was then FHN normalised relative to the frequency and power of \( f_0 \) for the frame itself. All frame FHN-spectra were then averaged to reinforce any shared pattern in each case.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Pathology</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>R</td>
<td>23</td>
<td>Pituitary stalk lesion</td>
<td>Nil</td>
</tr>
<tr>
<td>H</td>
<td>44</td>
<td>NF Pituitary adenoma</td>
<td>Pituitary Surgery &amp; irradiation</td>
</tr>
<tr>
<td>W</td>
<td>47</td>
<td>Macroprolactinoma</td>
<td>Pituitary Surgery &amp; irradiation</td>
</tr>
<tr>
<td>S</td>
<td>40</td>
<td>Craniopharyngioma</td>
<td>Pituitary Surgery</td>
</tr>
</tbody>
</table>

Table-1
Adult GHD cases, age at study, pathology and treatment (additional to endocrine replacement that includes testosterone for all patients and thyroxine for H, W & S).

The entire FHN, EGG spectral pattern for each individual was then characterised above \( f_0 \) using complexity analysis based on ApEn. Specifically the averaged FHN spectrum was truncated to produce a single new series extending from the first minimum to the 7th harmonic inclusive, taking logs and then computing the standard deviation \( \sigma \) of the result. In order to obtain the widest spread of ApEn, a \( k \) value of 0.6 was empirically determined for the computation of \( r \) in both normal and pathological cases.

IV. RESULTS

Normal Population: Spectral Complexity

Normal spectral patterns clearly separate into two ApEn complexity groups (Students two tail t-test \( p<0.001 \)).

The largest group, G1, had strong spectral features extending across the harmonic range within a slowly decaying spectral envelope. The smallest, G2, had weak spectral features that decayed rapidly towards the higher harmonics. Figure-1 shows the population averaged FHN for G1 and G2 populations. ApEn complexity analysis elegantly quantifies G1 and G2 differences. G1 has 55 individuals with high, mean complexity 0.34 (+/- 0.04). G2 has 30 individuals with low mean complexity 0.18 (+/- 0.05). Pitch analysis of EGG data showed no differences between G1 and G2, both having a mean \( f_0 \) of 122-124 Hz (+/- 29 Hz)

<table>
<thead>
<tr>
<th>Case</th>
<th>( f_0 ) (Hz)</th>
<th>Complexity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Males G1</td>
<td>124 (29)</td>
<td>0.34 (0.04)</td>
</tr>
<tr>
<td>Normal Males G2</td>
<td>122 (29)</td>
<td>0.18 (0.05)</td>
</tr>
<tr>
<td>R</td>
<td>172</td>
<td>0.35</td>
</tr>
<tr>
<td>H</td>
<td>154</td>
<td>0.18</td>
</tr>
<tr>
<td>W</td>
<td>118</td>
<td>0.18</td>
</tr>
<tr>
<td>S</td>
<td>117</td>
<td>0.09</td>
</tr>
</tbody>
</table>

Table-2
Fundamental frequency \( f_0 \) (standard deviation) and complexity for normal and pathological cases.

Adult Acquired GHD Cases: Spectral Complexity

Table-2 shows the spectral complexities and \( f_0 \) values for the 4 adult acquired GHD cases. The first row shows case R in which \( f_0 \) is 172 Hz, intermediate between normal male and female pitch. It is the only case in which the spectral pattern is strong and well maintained to high harmonic levels. The spectral envelope is clearly ‘bright’ but erratic with spectral envelope decay reversed twice. The complexity at 0.35 is typical of the G1 population. The remaining 3 adult acquired GHD cases have characteristically low, male \( f_0 \). Their spectra clearly exhibit the G2 decaying envelope and the pulsatile
reduction with increasing harmonic level. Progressing from case H to S there is the characteristic obliteration of spectral features by noise. Complexity levels are low and comparable to the G2 normals, particularly for case S, where there are few spectral features and a pathologically low ApEn of 0.09.

V. DISCUSSION

Three of four adult acquired GHD cases were middle aged. Hence larynx development was completed before onset of GHD. Their low complexity levels are comparable to the minority G2 male normal population. The membership ratio G1:G2 is 2:1 but this is more than reversed at 1:2, with one other case well below G2, in the adult acquired GHD cases and so is likely to be significant despite the small sample of cases. Life style, such as smoking etc., may be a possible cause. However, given the similarity of treatment regime in all three cases, these effects could conceivably have been produced by a reduction in conscious control over fold functionality. Conscious change of control has been demonstrated by Moore et al. [9].

The fourth GHD case, R, has high, G1-level complexity and a f0 bordering on female levels. Apart from endocrine replacement, R received no treatment. The onset of acquired GHD occurred after reaching final height but before full adult development in respect of body composition and bone mass. Environment and life-style are unlikely causes for this effect. Hence, perturbation of larynx development due to GHD is a potential explanation for these characteristics.

VI. CONCLUSION

There is at least initial evidence that adult acquired GHD, occurring between late puberty and adulthood could disrupt larynx development and be detected by EGG complexity analysis. Furthermore, this can be differentiated from post pubertal adult cases of acquired GHD, in which the result of treatment may be reduced conscious control of fold functionality and produce a measured EGG complexity that is comparable to the lowest G2 level of normality or pathologically low.

REFERENCES